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Chronic and Healed Miliary Tuberculosis of Lungs.—A distinction may be made between healed and chronic miliary tuberculosis of the lungs. Diagnosis is made only from the roentgenogram. The former term should be applied to the chest that shows in the roentgenogram calcified areas of tubercle, all of the same size, and the same degree of calcification and uniform distribution. Such lesions must be of the same age and must represent the residue of a healed, true miliary seeding of the organs. The second term, however, should be applied to the chest, the plate of which shows a miliary stippling of areas of different size and of different degrees of calcification, and therefore of varied age. Lesions of this type are obviously metastatic, but they have occurred not all at the same time, and represent a chronic form of miliary disease. Symptomatically, the former type of case may have been ill for a short time, while the other may be expected to have had a checkered sort of illness, characterized by repeated exacerbations or attacks of vague illness. Two such cases are reported.—*Chronic Miliary Tuberculosis and Healed Miliary Tuberculosis, M. I. Bierman, Radiology, February, 1926, vi, 165.*—(*H. S. W.*)

Localization of Miliary Tubercles in Human Spleen.—In a study of 16 human spleens, by methods of serial sectioning and reconstructions, it was found that splenic tubercle is situated with marked regularity in the white pulp. This localization seems to justify the view that the lymph follicle is the primary site of splenic tubercle and of the origin of the intoxicating substances.—*Die Lokalisation der miliären Tuberkelknoten in der Milz beim Mensche, E. Graberg, Virchow's Arch. f. path. Anat., 1926, cclx, 287.*—(*H. J. C.*)

Reaction of Pleura and Lungs to X-Rays.—An inflammatory reaction of the pleura and lungs to irradiation may occur in any case in which a sufficient dose of radium or roentgen-rays has been directed to those structures. The symptoms of pleuropneumonitis generally appear from

two to four weeks after a course of roentgen-ray treatment and consist chiefly of cough, shortness of breath, and sometimes fever. The physical signs vary considerably. During the acute stage, dry and moist râles in all degrees of pitch and volume can be heard over the affected lung. A distinct pleural rub is sometimes audible. Pleural effusion is known to occur with the more severe grades of irritative inflammation. The roentgenological signs may consist merely of the diffuse fog of inflammatory pleural thickening, or they may simulate those of the focal type of pneumonia so commonly seen after influenza. A differential diagnosis must often be made between diffuse metastasis and pleuropulmonary reaction to roentgen rays. In the former it is generally bilateral, whereas in the latter it is generally unilateral. In the roentgen-ray reaction there is a tendency to retraction of the injured lung and of the mediastinum toward the affected side. Roentgen-rays of short wave-length and the filtration employed are of minor importance in the production of pleuropulmonitic reactions. The chief factor is the dosage. Inflammatory manifestations in pleura and lungs are the more likely to supervene the nearer the dosage approaches, or passes beyond, the limit of normal skin tolerance.—*The Reaction of the Pleura and Lungs to Roentgen Rays, A. U. Desjardins, Am. J. Roentgenol. & Radium Ther., November, 1926, xvi, 444.*—(*W. I. W.*)

Pathology of Pleural Adhesions in Pulmonary Tuberculosis.—The subject has been approached from the standpoint of (1) postmortem material from the bodies of tuberculosis patients, and (2) experimental material from the inoculation of laboratory animals with tubercle bacilli. *Gross Necropsy Appearance:* The usual method of opening the thorax was modified as follows: The clavicle was sawed through at about the junction of the middle and outer thirds, and its inner two-thirds was removed along with the sternum. This gives a good view of the apical pleura *in situ*. Adhesions were found to form more over the posterior aspect of the ribs than anteriorly, where movement is greater. Narrow pedunculated adhesions are commonly found attached to cavities in the apex of the lower lobe, while broad, often cribriform, adhesions tend to follow a generalized inflammation of the visceral pleura. Adhesions may enclose a localized collection of fluid or form a thin plastic sheet over a spontaneous perforation or needle-puncture. Calcification of adhesions is rare. Complete calcification of the pleura has been seen encasing a fibroid lung. Occasionally fresh infection in the form of miliary tubercles is seen around an adhesion. The commonest site of adhesions was in the region of the apex, and especially its posterior aspect in the vertebral half. Right-sided adhesions were more often found to be tough and fibrous in consistence. Adhesions covered upper-lobe cavities in half the cases. Lower-lobe adhesions also often covered cavities. Interlobar adhesions were common, especially on the right side. *Histological Appearance:* The following are cited: (1) exudation of plasma on to the pleural surface, with migration of leucocytes and desquamation of endothelial cells; (2) formation of fibrin clot from plasma; (3) production of granulation tissue; (4) formation of new blood capillaries; and (5) development of connective tissue. The following definite signs of tuberculosis were found: (1) tubercle bacilli, (2) giant cells, and (3) small areas of caseation (one case). Tubercle bacilli were much more common in the granulation tissue than in the connective tissue. The subpleural elastic lamina was frequently spread out in the form of a loose skein and individual elastic fibres often extended around newly-formed blood capillaries. *Guinea Pig Experiments* were performed in the attempt to repeat Paterson's work, but somewhat divergent results were obtained. In 4 out of 12 animals adhesions were successfully produced. Again, on microscopic examination, the tubercle bacilli were present chiefly in the areas of granulation tissue. Occasionally bands of adhesions had a partial endothelial covering. *Conclusions:* 1. The character of pleural adhesions depends upon the numerous factors, such as position, movement, and the presence of tuberculous disease in subjacent lung tissue. 2. The order of frequency of location at autopsies was upper lobe, interlobar fissure, pericardium, lower lobe, diaphragm and mediastinal pleura. 3. The histological changes, in order, are exudation and endothelial proliferation, fibrin formation, granulation-tissue production, blood-capillary formation, and connective-tissue formation. In tuberculous lesions giant-cell formation and caseation occur, and, if an adhesion be ruptured at a point where tubercle bacilli can be liberated into the pleural sac, effusion usually ensues. This probably occurs from time to time in cases of induced pneumothorax. 4. Elastic tissue is found inconstantly, and appears to be derived from the subpleural elastic layer. 5. Pleural adhesions, experimentally induced in guinea pigs, showed stages of formation similar to those found in human lesions. Connective tissue was noted as early as the tenth day after infection.—*The Pathology*

of Pleural Adhesions in Pulmonary Tuberculosis, S. R. Gloyne, Tubercle, June, 1926, vii, 424.—(A. P.)

Accessory Phrenic Nerve in Animals.—The idea that section of the phrenic nerve is fatal for animals is not correct. The result varies, according as the animal's breathing is predominantly costal or abdominal. Unilateral section of the phrenic in the rabbit, which breathes exclusively abdominally has appreciable effect, but after bilateral section dyspnea occurs. The animal attempts to accommodate itself to the changed conditions by lying on its abdomen and respiring with the thorax. Even though the respirations are dyspneic the animals can remain alive for months in apparent health. In animals the matter of the varieties of the phrenic nerve is just as significant in producing paralysis of the diaphragm as in man. The varieties of the phrenic and accessory phrenic nerves are reviewed for the cat, rabbit and dog. From an anatomical standpoint phrenicoexairesis and intrathoracic phrenicotomy are equally indicated.—*Der akzessorische oder Nebenphrenicus beim Tier und seine praktische Bedeutung, E. Ruhemann, Beitr. z. Klin. d. Tuberk., 1926, lxii, 511.—(H. J. C.)*

Lymphatic Vessels from Thoracic Duct to Mediastinal Nodes in Dog.—There are described in the dog lymphatic vessels, furnishing direct communication from the thoracic duct to the right and left inferior thoracic and the right hilum lymph nodes. An active circulation occurs through these vessels from duct to nodes, which in addition anastomose with each other, with the lymphatics of the diaphragm, and with the inferior cervical nodes.—*Sur l'existence chez le chien de vaisseaux lymphatiques allant directement du canal thoracique à certains ganglions du mediastinum, L. Binet, Meeting, Soc. de Biologie de Paris, November 7, 1925, reported in Presse Méd., November 18, 1925, no. 92, 1527.—(E. H. K.)*

Intoxication in Tuberculosis Due to Tissue Products of Tuberculous Foci.—Caseated bronchial and mesenteric lymph nodes from animals and man, obtained shortly after death, were prepared with physiological saline solution and, after being tested for sterility, were used in rabbits to determine their toxicity. In addition, these extracts were used as antigens for Pirquet tests in tuberculous individuals. As a result of the study it is concluded that the toxemia of tuberculosis occurs in two forms, one a pure toxemia occasioned by the products of metabolism of the tubercle bacillus itself, and the other a toxemia caused by the absorption of toxic substances originating from the destruction of caseous tuberculous tissue. The caseous masses possess, in some cases, not only toxic but also antigenic properties. In some cases the blood of caseous tuberculosis cases contains, not antibodies, but the antigen (disintegration products of caseous tuberculous organs). Mixed infection does not play the rôle in tuberculosis previously ascribed to it.—*Zur Frage der caseösen Toxämie bei der Lungentuberkulose, A. R. Rosenberg, Beitr. z. Klin. d. Tuberk., 1926, lxiii, 132.—(H. J. C.)*

Physiology of Serous Membranes.—It has become customary to consider the pleural, pericardial and peritoneal cavities as wholly similar in functions and reactions, and this generalization is supported by most of the evidence. The present review, however, is presented largely from the standpoint of the reactions of the peritoneum, as it has been much more extensively studied than either the pleura or pericardium, because of its greater accessibility and its importance in so many surgical procedures. The joint cavities, bursae, tendon-sheaths and cerebrospinal spaces are omitted from this consideration. *Structure:* The mesothelial cells lining the serous cavities, sometimes called *endothelium*, were first carefully studied by Bichat, Henle and von Recklinghausen. The last-named introduced the study of cellular membranes by means of the silver-nitrate reaction and described certain pore-like openings which he called *stigmata* and *stomata*. This concept was accepted by some observers and disputed by others. Kolossow developed another method of staining with osmic acid and "developing" with pyrogallic acid and tannin. He described the mesothelial cell as a double plate, the inner portion being smaller than the outer, containing the nucleus, and connected with adjacent cells by fine anastomosing processes. He describes the entire mass of the lower mesothelial layer as a syncytial structure. MacCallum agrees with Kolossow and Muscatello that there are no preformed openings into lymphatics from serous cavities and that the mesothelial cells are connected by processes. Hertzler, on the other hand, finds evidence of a cement substance between the cells, and Lewis's recent work indicates the absence of actual connection. Most of those who have studied the finer characteristics of these cells agree that they are bound together in some way, and the most rational view at present is that they are distinct cellular entities, which may, how-

ever, have some close type of association. *Histogenesis:* Many workers have concluded that mesothelial cells and fibroblasts are functionally interchangeable, but a few have denied any close biological relationship. Cunningham has found that progressive morphological changes from flat to columnar and tall cuboidal forms occur as a result of irritation. He finds certain characteristic reactions to certain dyes, and concludes that the new cells are always produced from pre-existing mesothelial cells and belong in a group distinct from fibroblasts, to which, however, they are probably more closely related than are either to phagocytic mononuclears. The question also arises as to the relationship between the mesothelial cells and the free mononuclear cells found in serous exudates. Of the work done on peritoneal exudates that of Pappenheim and Fukushi is the best. Pappenheim considered all possible sources from which free exudate cells might be derived, and eliminated all except the polyblastic clasmatocytes and adventitial cells of the omentum and subserosal tissues. The staining reactions with trypan-blue and other vital stains also differentiate peritoneal mesothelial cells from the macrophages of peritoneal exudates. Cunningham found that desquamated serosal cells degenerate and never become phagocytic mononuclears. Cunningham, Sabin and Doan have differentiated two types of phagocytic cells, *monocytes* and *clasmatocytes*, in the rabbit, on the basis of reaction to supravital dyes. *Absorption of Particulate Material:* MacCallum found no evidence that material placed upon the eviscerated diaphragm flowed into submesothelial spaces through apertures, but was able to demonstrate large phagocytic, mononuclear cells making their way between the mesothelial cells into the lumina of lymphatic lacunae. He thought the transference of cells and contents was considerably affected by the respiratory movements, and postulated, instead of preformed openings, potential openings dependent upon cellular contractility or lack of expansile power. In turn, however, following the later work of Cunningham and others, this hypothesis is being replaced by one which assumes that most, if not all, particulate material absorbed from the peritoneal cavity passes directly through the living mesothelial cytoplasm. *Absorption of Solutions:* In general, the earlier workers accepted the view that the peritoneal cavity is a part of the lymphatic system, but the important work of Heidenhain indicated that the absorption of fluids takes place principally by way of the blood-vessels. Starling and others confirmed this, but later Adler and Meltzer, on the basis of experiments with strychnine and potassium ferrocyanide, returned to the earlier concept. Still later, Dandy and Rowntree, and Shipley and Cunningham pursued the study, and it now seems wholly settled that solutions absorbed from the peritoneal cavity pass in large part directly into the blood-stream, and in smaller measure into the lymphatics. Starling and Tubby, working with the pleura, found that dyes appear much more quickly in the urine than in the lymph and in much larger quantity. Starling, however, believes that isotonic solutions are absorbed via the lymphatics, and Bolton extends this to include serum. While the laws of osmosis and diffusion play a great part, recent exact work indicates some activity of the mesothelial cells themselves. *Practical Applications:* Blackfan and Maxcy utilized the peritoneal route for introducing solutions of sugar and sodium chloride into infants in whom venipuncture is difficult. These infants responded equally well. The use of the peritoneal route for the administration of whole blood has been suggested. Blood so introduced disappears rapidly, but some clotting in the recesses occurs. The rate of absorption is, of course, slower, but a rabbit can absorb about one-fifth of its blood-volume in four hours. Narat has found the introduction of a 20 per cent glucose solution in animals definitely bactericidal and worthy of trial in human peritonitis. Douglas has suggested the intraperitoneal use of adrenalin to reduce toxic absorption. Further studies should be directed along clinical lines.—*The Physiology of Serous Membranes, R. S. Cunningham, Physiol. Rev., April, 1926, vi, 242.*—(*A. P.*)

Absorption from Lower Respiratory Tract.—The problem of absorption confronts scientific investigation in practically every field of human endeavor, and *in vitro* explanations alone are inadequate, the problem resolving itself into the solution for a complicated cellular mechanism. The route of absorption of fluids from the serous cavities is by way of blood and lymph-vessels, and the state of solution is important. The rôle of special cells, such as clasmatocytes and monocytes, is referred to. Particulate matter in the pleura, according to the studies of Karsner and Swanbeck, is taken up by endothelial cells *in situ*, and the parietal pleura appears to be more active than the visceral. Drainage from the parietal pleura is chiefly into mediastinal lymph nodes, from visceral into hilum nodes. Respiratory movements alone may propel the material through the lymph channels. The rate of absorption of solutions, both for peritoneum and pleura, is equal in all

postures except pelvis down, when it is 13 to 15 per cent less. Katsura believes that crystalloids are absorbed by the blood, colloids by the lymphatics. Corper and associates, after preliminary tests with various substances, especially dyes, found that only one dye, indigo-carmine, fulfilled requirements, and they finally discarded even this in favor of sodium sulphocyanate, which in intracutaneous tests proved to be without perceptible injurious effect on tissues in 2 per cent concentration. The rate of absorption of 2 cc. of a 2 per cent solution from the lungs after intratracheal injection was determined by colorimetric quantitative methods. This rate was found to exceed that of absorption from normal pleural, peritoneal or subcutaneous tissues. In order to determine the effect of acute inflammatory conditions in the lungs and pleura on absorption, a series of guinea pigs was given injections of 2 cc. of 0.2 per cent hydrochloric acid and 2 cc. of 0.2 per cent mercurochrome into the right pleura, and another series was given inhalations of bromine vapor, which produced an acute pneumonitis, usually with gradual recovery. A decided retardation of absorption was found in all these instances. On the other hand, induction of artificial pneumothorax in the absence of inflammatory conditions did not affect absorption. *Summary and Conclusions:* In brief these are as follows: Absorption and resorption of liquids from the lower respiratory tract, lungs and pleura, follow the main principles of absorption in other parts of the human economy. The rapidity of absorption of crystalloids from the lungs and pleura exceeds that from peritoneum and subcutaneous tissues. The rapidity of absorption of liquids from the lungs is probably largely accounted for by this vascularity and the large total alveolar surface. Acute inflammatory conditions produced in the pleura by chemical means retard the absorption of crystalloids, but this is not influenced by artificial pneumothorax instituted shortly before.—*Absorption from the Lower Respiratory Tract Under Normal and Pathologic Conditions, H. J. Corper, J. Am. M. Ass., June 5, 1926, lxxxvi, 1739.—(A. P.)*

Lactic-Acid Content of Pathological Effusions.—Pleural transudates have the same lactic-acid and sugar concentration as has blood. In sterile lymphocytic and leucocytic effusions the lactic-acid concentration varies from 17 to 32 mgm. per cent, according to the age of the effusion. In tuberculosis and suppurative infections of the pleura, as well as in the exudate with tumors, sugar is absent from the fluid, and lactic acid is present in great amount. In the fluid of ascites due to tumor a high lactic-acid value occurs, without noticeable change in the sugar value. Transudates, pleural exudates and ascitic fluid, in the absence of suppuration, do not cause glycolysis.—*Ueber den Milchsäuregehalt pathologischer Ergüsse, R. Scheller, München. med. Wchnschr., November 5, 1926, lxxiii, 1879.—(E. R. L.)*

Calcium Content of Saliva in Relation to Diet and Tuberculosis.—The present investigation was carried out with the following ideas: (1) to see whether there is any relation between the amount of calcium in the saliva and the development of dental caries; (2) to determine whether it is possible readily to alter the calcium content by varying the diet; and (3) to determine the effect of tuberculosis upon the salivary calcium. Mellanby and Pattison previously showed that by raising the amount of fat-soluble vitamine in the diet the spread of caries could be delayed. Pattison now shows that by increasing this vitamine the salivary calcium is raised. *Technique:* Saliva was obtained by asking patients to spit into glass tubes three minutes after their mouths had been washed out with water. Various methods of estimation were employed, and the results were recorded by Laidlaw and Payne's alizarin method, and the Kramer-Tisdall method. *Influence of Diet:* Two definite diets were used, of which one (*A*) was rich in vitamine A, and the other (*B*) was more farinaceous in character. All patients on diet *A* showed a much higher average calcium content, which persisted after their diet was discontinued, probably due to a storage of vitamine A. It was found possible to increase the calcium content of patients on diet *B*, by changing to the ordinary hospital diet, and still more by giving diet *A*. *Influence of Other Factors:* The average calcium content of all the children on admission was low, about 4.77 mgm. per 100 cc. as compared to a normal of 6 to 12 mgm. per 100 cc. All the children suffered from bone and joint tuberculosis, with various degrees of decalcification. Those with disease of longest standing had the lowest calcium content. Also, the Sheffield water is low in calcium, and a comparison of Sheffield with London residents showed a distinctly lower calcium content. Children living in districts supplied with hard water were found by Rose to suffer less from caries than those where the water was soft. *Summary:* 1. The salivary calcium content is influenced by diet. A high calcium content can be produced by a diet having a large fat-soluble vitamine

content and a low calcium content by a diet containing much cereal, especially oatmeal and comparatively little fat-soluble vitamine, even though the amount of calcium ingested may be as great as that in the first diet or exceed it. 2. The salivary calcium content is not increased by increasing the calcium of the diet over a short period. 3. Tuberculous children appear to have a lower calcium content of the saliva than normal children, and, on the whole, low resistance to this infection is accompanied by low calcium content. 4. The calcium content of the saliva is controlled by the same factors of special nutrition as those on which the calcification of teeth and bones depends.—*Dietetic Conditions Which Influence the Calcium Content of Saliva: the Possible Significance of these Facts in Tuberculosis, C. L. Pattison, Brit. M. J., July 3, 1926, no. 3417, 6.—(A. P.)*

Effect of Menstrual Alterations on Capillary Permeability in Tuberculosis.—A series of observations on a group of normal young women show that in the premenstrual period the blister-time is shortened, the skin tonus being parasympathetic; during menstruation the skin tonus returns to normal and the internal organs become parasympathetic; in the intermenstrual period the blister-time is longer, and there is an average capillary permeability of 0.72, as compared to the premenstrual of 0.75 and the menstrual of 0.77. Just before and during menstruation the blood-pressure is higher than in the intermenstrual period. These changes in capillary permeability may explain the direct influence of the menstrual cycle on tuberculosis, the tuberculous women during menstruation frequently showing evidence of focal activation and apparently being less resistant to the infection. In the presence of a tuberculous focus, an increase of capillary permeability has an effect comparable to a tuberculin injection, the exchange of material to and from the focus being accelerated, with a consequent liberation of tuberculin. The first days of menstruation are particularly favorable for a rise in temperature, because at this time the skin tonus returns to normal, and heat is dissipated less rapidly than before. Menstruation represents a biological rearrangement involving an endocrine change, an ionic change, and an alteration in autonomic nervous control, these three changes forming the vegetative control of the tissues and being fundamental factors in thei reaction to infection. The menstrual cycle, being one of vagotonia, therefore makes for less favorable conditions of resistance to tuberculosis.—*The Relation of Menstruation to the Permeability of the Skin Capillaries and the Autonomic Tonus of the Skin Vessels, W. F. Petersen and G. Milles, Arch. Int. Med., December 15, 1926, xxxviii, 730.—(G. L. L.)*

Influence of Lung on Coagulability of Blood.—The passage of the blood through the lungs renders it less coagulable. This is demonstrated by the following experiments: (1) In comparing venous blood from the right side of the heart with blood from the carotid artery, the former is found to coagulate more quickly. (2) After intravenous injection of peptone the resulting diminution in coagulability is more marked in the carotid blood than in that of the right side of the heart. (3) If an injection of peptone has rendered the blood incoagulable, the return of coagulability appears first in the blood of the right side of the heart. It is not the carbon dioxide that renders the venous blood more coagulable, since extreme asphyxia does not appreciably alter this factor.—*Action du poumon sur la coagulabilité du sang, H. Roger and L. Binet, Meeting, Soc. de Biologie, October 17, 1925, reported in Presse Méd., October 24th, 1925, no. 85, 1417.—(E. H. K.)*

Hydrogen-Ion Concentration of Blood in Tuberculosis of Guinea Pig.—As long as tuberculosis remains localized in the guinea pig the H-ion concentration does not change appreciably from the normal of pH 7.32. With generalization of the disease and involvement of the spleen and liver an alkaline trend occurs, the pH reaching 7.45.—*Die Wasserstoffionenkonzentration im Blute bei experimenteller Meerschweinchen Tuberkulose, F. Schmidt, Ztschr. f. Immunitätsforsch. u. exper. Therap., March 12, 1926, xlvi, 386.—(E. R. L.)*

Cholesterinemia of Pregnancy in Tuberculous Women.—A condition of hypercholesterinemia is usually attributed to pregnancy and a hypocholesterinemia to febrile tuberculosis. What is the rôle of each of these conditions, the one physiological, the other pathological, and how do they interact upon each another? Can a study of the cholesterin content of the blood aid in prognosis when tuberculosis and gestation develop together? The large number of tuberculous women studied divide themselves into three groups, the cholesterin content of the blood having been determined: (1) simply during the pregnancy, (2) after delivery, and (3) both before and after delivery. As a control, cholesterin was determined similarly in normal women, in others with pulmonary tuberculosis but

not pregnant, and in still others who were pregnant but not tuberculous. The chemical method employed was Grigaut's. *Conclusions:* In pulmonary tuberculosis the cholesterin content of the blood undergoes changes related to the evolution of the disease. Hypocholesterinemia is found almost always in the severe forms with temperature elevations and depends more upon the activity of the lesions than upon their extent. In tuberculous women the cholesterinemia during and after pregnancy varies according to the form of the tuberculosis. In arrested cases the changes are those met with in the course of normal pregnancies and deliveries. In progressive forms of tuberculosis, on the contrary, there is a moderate hypercholesterinemia, which is followed after accouchement by a notable and persistent fall in the quantity of cholesterin. The content of cholesterin in the blood may therefore give valuable information as to prognosis in tuberculous women, who are either pregnant or have been recently delivered. A study of the relation of allergic reactions and arterial tension to the cholesterin content of the blood in pregnant women and in other tuberculous persons indicates that no relationship exists between cholesterinemia, anergy to tuberculin and arterial pressure.—*La cholestérinémie de la grossesse chez les femmes tuberculeuses, Salomon and Potter, Ann. d. Méd., 1926, xix, 587.*—(*W. B. S.*)

Serum Cholesterol of Guinea Pigs.—The literature offers certain suggestions that changes in the distribution of cholesterol may be a feature of the pathology of tuberculosis. The authors cited agree that the blood cholesterol is decreased in the more advanced stages of tuberculosis. In the earlier stages normal or increased values have usually been found. This refers to human beings and rabbits. No references were found on blood-cholesterol determinations on normal or tuberculous guinea pigs. In view of the variation in natural resistance existing among inbred families of guinea pigs, it seemed not impossible that these animals might show differences referable to their cholesterol metabolism. A stock of inbred guinea pigs, from the same families used by Wright and Lewis, and Lewis and Loomis, were furnished by Lewis for these experiments. The experiments were planned to determine the effect of infection with bovine tubercle bacilli on the cholesterol content of the serum, and also to determine the normal content of the different inbred families. Observations were confined to males because of the large individual variations among the females. Sixteen males from inbred *family 35* and the same number from inbred *family 13*, were bled from the heart, the blood pooled and allowed to clot in the refrigerator. The cholesterol content of the centrifugated serum was determined by Bloor's method with slight modification. Before infection *family 35* showed an average cholesterol content of 67 mgm. per cent and *family 13*, 58 mgm. per cent. The diet was changed from hay, oats and mangels, to hay and soaked oats daily, and cabbage once a week. The change was without effect on the cholesterol content of the serum. After infection with 0.1 mgm. of bovine tubercle bacilli intraperitoneally, the average cholesterol content of *family 35* was 67 mgm. per cent, and *family 13*, 58 mgm. per cent. A further series of determinations were made on four inbred families, *13*, *35*, *32* and *2*, to determine the influence of diet. Before the change of diet the average cholesterol findings were, 57, 66, 62.5 and 50 mgm. per cent respectively. The change was made after the first bleeding and two weeks before the second. The second series of determinations showed 55, 65, 66 and 52.2 mgm. per cent. The individual variations of the cholesterol content of the serum of 4 guinea pigs from *families 13* and *35* were studied. *Family 13* showed 50, 48, 50 and 52 mgm. per cent, and *family 35*, 63, 58, 59.5 and 58 mgm. per cent. *Summary:* 1. Infection with bovine tubercle bacilli produced no alteration in the serum-cholesterol content in guinea pigs. 2. Certain controlled variations in diet produced no changes in the serum-cholesterol content in guinea pigs. 3. Inbred families of guinea pigs known to manifest differing resistances to tuberculosis gave differing serum-cholesterol values, but no direct relationship between the two sets of phenomena could be established. 4. It seems probable that in the guinea pig the cholesterol content of the blood serum is influenced by inherited factors.—*The Quantity of Cholesterol in the Blood Serum of the Guinea Pig as an Inherited Character; Its Relation to Natural Resistance to Tuberculosis and to Tuberculous Infection, R. E. Shope, J. Exper. M., January 1, 1927, xlv, 59.*—(*F. P.*)

Metabolism and Nutrition in Tuberculosis.—This is an extensive review of the literature on metabolism and nourishment in tuberculosis, including a consideration of diet. It is a continuation of a similar review presented in 1923 by the same author.—*Ergebnisse oder Übersichtsberichte. Neuere Ergebnisse der Stoffwechselkunde und der Ernährung bei der Tuberkulose, H. Schulte-Tigges, Centralbl. f. ges. Tuberk.-Forsch., 1926, xxv, 721.*—(*H. J. C.*)

Gaseous Metabolism in Pulmonary Tuberculosis.—Brieger corroborates the observations of Gräfe, that afebrile cases of phthisis have an increased basal metabolism and that pyrexia has no definite influence on the daily basal-metabolism curve. In phthisis the inhalation of oxygen reduces the depth of respiration and gaseous metabolism, as compared with healthy individuals. In tuberculosis there exists an oxygen deficiency. Oxygen want in the nervous centres is viewed as a not insignificant factor in the basal-metabolism increase. Pyramidon does not prevent the increased gaseous metabolism. It is concluded that oxygen inhalation is indicated in phthisis even though it acts only during the period of actual inhalation. Even mild bodily exertion increases the respiration and gaseous metabolism, according to the severity of the case. The rest cure favorably influences respiration and gaseous metabolism. For evaluating the activity of a tuberculosis case, as related to the gaseous metabolism, the following is outlined: A normal gaseous metabolism does not exclude an active process, and the gaseous-metabolism increase parallels to a certain extent the severity of the disease. Careful observation of the gaseous metabolism during graduated bodily exercise can provide an index of the ability of the patient to carry on work.—*Die Bedeutung der Gaswechseluntersuchung für einige Fragen der Pathologie und Therapie der Lungentuberkulose, E. Brieger, Beitr. z. Klin. d. Tuberk., 1926, lxiii, 403.*—(*H. J. C.*)

Vital Capacity of Negro Race.—The vital capacity of 539 white children corresponded to Stewarts' standard curve. The vital capacity of 397 negro children, as compared to the white, was markedly and consistently lower in all age groups from 6 to 17 years. There were no physical defects in any of the children studied. White and negro adults were similarly studied. The vital capacity of the negro, when calculated from sitting height, is higher than when determined from standing height or surface area. The standard deviation and coefficient of variation in both races is lowest when the vital capacity is studied from surface area. *Conclusions:* 1. The vital capacity of the negro race, in both sexes and for all age-groups studied (6 to 65 years), is markedly lower than the vital capacity of the white race. When calculated from the surface area the difference is from 15 to 20 per cent in children, and from 25 to 35 per cent in adults. 2. The growth curves of weight and of standing height of white and negro children correspond closely, but negroes have a shorter trunk-length than whites. When vital capacity is calculated from stem-length, therefore, there is less discrepancy between the vital capacity of the two races than when it is calculated from surface area or standing height, the results being only 10 to 15 per cent lower than in the whites.—*Vital Capacity of the Negro Race, W. G. Smillie and D. L. Augustine, J. Am. M. Ass., December 18, 1926, lxxxvii, 2055.*—(*U. E. Z.*)

Analysis of Bacterial Allergy.—In the study of hypersensitiveness a differentiation has been gradually developed between the phenomena concerned in true anaphylaxis to the coagulable proteins, in which it is generally assumed that a true antigen-antibody union in the cells of the body underlies the responsible mechanism, and the many other manifestations of hypersensitiveness in which no such specific antigen-antibody relationship has been demonstrated. Although the tuberculin reaction represents the most extreme example of bacterial allergy, and is easily amenable to experimental study, certain difficulties made it necessary to study other bacteria in addition to tubercle bacilli and their products. The staphylococcus, streptococcus, typhoid bacillus, *Bacillus abortis bovis* and pneumococcus were chosen, thus including microörganisms of many degrees of solubility and of far greater potency for free antibody production than the *Bacillus tuberculosis*. The work reported in the present paper takes its departure from the following premises with regard to the tuberculin reaction: (1) The tuberculin reaction is independent of general anaphylaxis to tuberculoprotein. (2) Tuberculin hypersensitiveness in its extreme form cannot be induced by dissolved extracts of the tubercle bacillus which have been filtered (Berkefeld) to remove formed particles. It can be characteristically induced, not only by infection with living bacilli, but by treatment with dead bacilli, even after these have been boiled. These facts confirm the importance of typical tissue reactions, spoken of as tubercles, in the mechanism of tuberculin sensitization. (3) The mechanism of tuberculin reactions is independent of the presence in the animal body of precipitating or agglutinating antibodies. 4. Conversely, the substance in tuberculin responsible for the reaction in the sensitized animal is chemically separable from the precipitable residue carbohydrate fraction, and is probably a nitrogenous substance, perhaps a form of protein. The different types of skin response to the injection of bacterial substances were classified as follows as a

working basis: (1) The purely toxic reaction which has no direct connection with allergy and which is due to the primary toxicity of the injected material (Schick and Dick tests). (2) The immediate urticarial skin reaction which fades promptly. In man this is regarded as indicating protein sensitization. In guinea pigs the reaction plays a minor rôle in some of the phenomena of bacterial allergy. (3) The delayed skin reaction, which begins in five to six hours and reaches its highest development within eighteen to forty-eight hours, and which is characterized not only by edema but by inflammatory changes. These reactions do not go on to central necrosis or the central hemorrhages. This is the common type of reaction obtained in both man and guinea pigs with bacterial products, and sometimes occurs with protein sensitization. The classical tuberculin and abortion reactions probably consist, in part, of reactions of the type 3 class, but superadded there is tissue injury with hemorrhage and sometimes necrosis. The frequency of severe central cell injury and necrotic changes in relatively small reactions of the tuberculin type, as contrasted with the absence of these even in large reactions of the preceding class, suggests that a factor is present which is absent in the former. The experimental part of the article is devoted to the determination of the degree of specificity of bacterial allergy, which is of great importance; to attempts at active and passive sensitization to the carbohydrate residue (soluble specific substance) which were uniformly negative; to the relationship of the bacterial nucleoprotein and its antibodies to the allergic reaction; to attempts at passive sensitization to the bacterial nucleoprotein fraction; and finally to the tuberculin reaction itself. The last series of experiments include studies on the action of tuberculous tissue upon old tuberculin. From these experiments the fact that the so called bacterial allergies are dependent upon a mechanism, which differs materially from that determining true protein anaphylaxis, was confirmed. Anaphylaxis to the protein substances of bacteria probably occurs, but plays a relatively unimportant rôle in the phenomena of infection. The bacterial allergies, however, are of great importance, since they develop rapidly and render the infected animal highly vulnerable to products of the bacterial growth which are relatively innocuous for the normal animal. Neither the type-specific carbohydrate "residue antigens" nor the antibodies (agglutinins, precipitins, sensitizers, etc.), reacting with them, play any part whatever in bacterial allergy, and allergy is in no way related to that phase of resistance which is determined by these antibodies. Allergic hypersensitiveness seems to be related to other factors of resistance more definitely associated with cellular rather than intravascular reactions. It was found that guinea pigs could be actively sensitized with all the bacteria studied when repeated injections of whole bacteria or of the protein (nucleoprotein) fraction were administered. Large amounts of the latter are necessary, since these materials are indifferent antigens, possibly because of the severe manipulations necessary in their production. Sensitiveness develops usually in ten days after the first dose, and increases with continued treatment for three or four weeks. Hypersensitiveness is relatively specific, although not absolute, as highly sensitive animals show considerable overlapping. Continued treatment in considerable dosage leads to gradual desensitization when there are no chronic foci present, which would tend to continue the sensitization. Attempts at passive sensitization were irregular and inconclusive. When present, it appeared late and was of doubtful specificity. Attempts to neutralize the activity of the active allergic constituents of bacterial extracts, by incubation with any type of immune serum, also failed. Failure was also recorded in the attempt to show any increased fixation of tuberculin material on the part of tuberculous tissues or on that of living tuberculous animals. On the other hand, definite, although irregular, evidence was obtained that the incubation of O. T. with fragments of tuberculous lung tissue (less clearly with other tissues) leads to the formation of a substance that produces allergy-like lesions in the skin of normal guinea pigs. With somewhat greater regularity O. T., so treated, showed a higher potency for tuberculous animals. There was evidence that the factor responsible for this action was not easily separable from the cells themselves. When these experimental data are analytically considered in relation to the tuberculin reaction, a few outstanding and sufficiently reliable facts are noted, which compel the following limited definite deductions: There is no question of the complete independence of the true allergic phenomena from the ordinary bacterial antigen-antibody reactions. We know that the allergic substance is chemically separable from the carbohydrate "residue" or haptophore group of the bacteria, and is either a protein in itself or closely associated with bacterial protein. From the distinct, though limited, specificity of the allergic sensitiveness, it is evident that we are dealing with an immunological process in which the tissue cells acquire an increased specific capacity to react with this nitrogenous material, a capacity, which, in principle, is not far removed from the supposed "sessile receptor"

apparatus which is conventionally held responsible for protein anaphylaxis; and the analogy is further amplified by the apparent desensitization which continued treatment produced in many of the experiments. However, the analogy with protein anaphylaxis ends here. Passive sensitization with any form of immune serum or with the sera of highly sensitized animals is either feeble or entirely unsuccessful and indicates quite convincingly that, whatever the receptor apparatus of the cells may be, it is not easily given up to the blood-stream as are ordinary antibodies. From the tissue-tuberculin experiments it was learned that: (1) Contact with the tissues of tuberculous animals results in the production of a toxic factor, not unlike the autolytic toxic materials of some bacteria. (2) The active cell constituent, by which this action is wrought, is not easily separated from the cells, even by energetic methods of extraction. The process of allergy, then, may be conceived as follows: A nitrogenous (probably protein) constituent of the bacterial growth or of its body substance stimulates a specific reaction in the tissue cell by which its (the cell's) specific capacity to establish contact with this constituent is enhanced. The cell is thereby enabled to exert a probably enzyme-like effect upon this material in consequence of which a toxic substance is liberated, largely upon or possibly within the cell itself. Both processes may be dependent upon one and the same reaction-body, and are closely associated with the cell, and the factors by which the reaction is brought about are not easily given up to the blood-stream as are the antibodies formed in response to the injection of proteins or whole bacteria. The immunological mechanism described has some close analogies to those in which circulating antibodies are formed, but differs from these mainly in the intimacy with which the entire reacting system is associated with the cells themselves. There seems to be a definite relationship between this functional cell alteration and the phenomena of susceptibility or resistance.—*An Experimental Analysis of Bacterial Allergy, H. Zinsser and T. Tamiya, J. Exper. M., December 1, 1926, xliv, 753.*—*(J. S. W.)*

Influence of Measles on Allergy.—A number of investigations of the effect of measles upon various reactions, such as vaccination, the Wassermann and Widal tests, etc., indicate that measles exercises a sort of retarding influence. The temporary disappearance of the tuberculin reaction in measles may be regarded as an example of this general phenomenon; it is not an isolated fact, although it is only in measles that the phenomenon is encountered with such sharpness and constancy. The authors were not satisfied with the work done on the fundamental fact itself and have investigated the phenomenon from different points of view in 229 infants. In all, more than 1,000 Pirquet tests were performed. *Results:* 1. The reaction becomes negative before or during the eruptive phase of measles. It may disappear suddenly or gradually. In a study of 35 cases the reaction was found to reappear one week or more after the beginning of the eruption. Occasionally the anergy may continue longer, even to several weeks or several months. The reappearance is gradual, as shown by series of reactions. Three infants (8 per cent of the cases) continued to give a positive reaction throughout the measles, but the reaction developed much more slowly than normally, not reaching its acme until the fifth or sixth day. 2. The disappearance and reappearance of the power to react is neither faster nor slower in progressive than in latent tuberculosis. On the other hand, skin reactions regain a good intensity less rapidly in progressive tuberculosis than in the latent variety. 3. When reactions are repeated only every week or two, there is no modification of one test by another; but if the reactions are performed every day or two, the effect of the first reactions is unquestionably to increase the intensity of the subsequent reactions. 4. Eight cases of chicken-pox were followed. In three out of four a positive reaction became negative. In three infants the reaction remained positive throughout the disease. 5. The severity or mildness of the measles is the factor which plays the greatest rôle in the disappearance or reappearance of the power to react. Finally, since the temporary disappearance of the power to react to tuberculin introduced by skin scarification is only one of several indications of the retarding effect of different pathological conditions on certain reactions of the body, it does not appear justifiable to associate this phenomenon with the known phthisiogenic action of measles, an association whose importance appears to have been exaggerated.—*Recherches sur la disparition de la cuti-reaction positive à la tuberculine pendant la rugeole, Debré and Papp, Ann. d. Méd., Paris, 1926, xix, 576.*—*(W. B. S.)*

Tuberculin Reaction and Anaphylaxis.—Anaphylaxis appears to differ from hypersensitiveness to tuberculin in two important particulars, namely, (1) tuberculin hypersensitiveness cannot be produced by injection of tuberculin and (2) passive transference of hypersensitiveness to tuberculin from sensitive to normal animals probably

cannot be accomplished, despite the claims of several investigators to the contrary. From results in guinea pigs that have been injected with dead tubercle bacilli, it may be deduced that tuberculin must contain some element of bacillary protoplasm that is antigenic, "that is, capable of rendering guinea pigs susceptible, not alone to the compound as it exists in the bodies of the bacilli, but probably to any related compounds containing the specific reacting principle, which is in the tuberculin and which exists there in such a form that it can bring forth a reaction but cannot induce a state of sensitiveness. If such a supposition were true it would mean merely that in tuberculosis, while a whole protein or a true antigen, as in anaphylaxis, perhaps is required to produce the state of allergy, the sensitiveness which results is directed not toward the compound as a whole but to a special portion or radical of it, and that other compounds containing the same radical or perhaps even the specific radical alone are capable of eliciting a specific response." So we are justified in thinking of the mechanism of the tuberculin reaction as resembling that of anaphylaxis. The continuous production of specific antigen from the focus of infection sensitizes the body, and the antibodies become attached to certain of the body cells. When tuberculin is introduced into such an animal, the antibodies combine with the specific element or substance in the tuberculin, causing a local inflammatory or general reaction, either by mechanical irritation or by formation of a toxin.—*Anaphylaxis and the Tuberculin Reaction, M. Dorset, J. Am. Vet. Med. Assn., September, 1926, lxix (n. s. xx), 711.–(H. S. W.)*

Changed Constitutional Reaction to Tuberculin.—This is a report of the occurrence of a positive tuberculin reaction becoming negative in three different patients. The first case was that of a young man in good general condition, whose chief complaint was a persistent, slightly painful, obscure affection of the wrist. The decided positive constitutional tuberculin reaction obtained led on careful physical examination to the discovery of slight but distinct abnormal physical signs at the right apex. Acting on the assumption that this man harbored a tuberculous focus, which, for the time being, was causing no disease in a clinical sense, thorough treatment, specific and otherwise, was carried out for twelve months. The specific treatment consisted of the subcutaneous injection of progressively increasing doses of B. E., beginning with approximately 0.001 mgm. and ending in about eleven months, with 4 cc. (20 mgm.); it was carried out more or less in accordance with Koch's final directions for this treatment. The remainder of the treatment was ordinary general care at home. Seventeen months from the conclusion of specific treatment having been allowed to elapse, the second test was made for the purpose of comparison. It was completely negative. This series of events was repeated in a girl, who gave a positive reaction to 0.002 and 0.0002 mgm. T. K. but had no evidence of clinical pulmonary tuberculosis. Constitutional and specific treatment was carried out, the maximum dose of B. E. on this occasion being 0.4 cc. After fourteen months from the conclusion of specific treatment the test was repeated, with a negative result. A third case, showing similar altered constitutional reaction to tuberculin after specific and general treatment, is described. A constitutional reaction to tuberculin is a matter of very great practical importance, as it is capable of revealing disease at a time when it can be comparatively easily dealt with, and when specific treatment with large doses of tuberculin is easy, safe, and effective.—*Three Cases of Changed Reaction to Tuberculin from Positive to Negative, R. Carswell, Brit. M. J., October 16, 1926, no. 3432, 682.—(B. T. McM.)*

Effects of Tuberculin on Leucocytes, Allergy and Red-Cell Sedimentation.—Twenty-eight patients in various stages of tuberculosis were examined. The Van Ruck preparation of tuberculin was used. Every patient was examined three times in regard to the behavior of skin sensitiveness, leucocyte formula and red-cell sedimentation rate. This was done twenty-four hours before, during, and two or three days after the reaction following the subcutaneous injection of the tubercle-bacillus preparation. Nine normal control cases were also examined. The dosage of extract used varied according to the different hypersensitiveness of the subject. Five of the control cases reacted with a moderate rise of temperature, one with a higher rise, and the rest remained normal. The sedimentation rate measured after three hours was normal, but very close to the borderline. After the injection only one case showed a material change in skin hypersensitiveness, and this person had shown marked hypersensitiveness to small doses. Although there are great differences in the extent of skin sensitiveness in normal persons, they have no real tendency to be influenced by the application of the doses sufficiently large to cause a reaction. In 5 cases there was a slight elevation in the total white-cell count, 12,000 to 15,000, usually

associated with a rise in temperature but not always. A slight elevation in the white count, with an increase of neutrophiles and decrease of lymphocytes, without change in the neutrophilic formula (Arneth-Schilling), is considered the type of reaction of normal people. A greater or lesser rise of temperature was observed in 17 of the 28 cases studied. In some cases the temperature remained normal, and a real change in the sedimentation rate was seen. In others the sedimentation rate did not change, but the temperature showed a little elevation. A focal reaction occurred in only 10 of the 28 cases. There was a decided difference in the sedimentation rate in cases of the first, second and third stages, especially in the treated cases. Higher values were observed in the third stage and in the progressive types of the first and second stages. By observing the rate of sedimentation a definite differentiation between the stages could not be established. Five types of sedimentation were observed during the reactions following the administration of the bacillary extract. In the first type the curve corresponds to the normal, which has no tendency to be accelerated, only reaching a higher level. To this group belong some of the first-stage patients in good physical condition, afebrile and fibrotic, and those with tuberculosis of the lymph nodes, also a progressive case in the first stage, which improved later, and those of the third stage that had been under treatment for a long time and had become desensitized, had gained in weight and whose disease was inactive and stationary. The second type shows an acceleration only in the third hour. Here belong the fibrotic and exudative and the rapidly improving cases of the first stage. Type three represents curves, the rise of which begins in the first hour and slowly reaches its highest level in the second and third hours. It represents the exudative cases of the first and second stages with good prognosis and the favorable stationary cases with a tendency to be progressive in the third stage. Type four shows an acceleration from the second hour on, and most marked in the third hour. Here belong cases from the borderline of the second and third stages and an exudative case of the first stage which was always subfebrile. Type-five curve represents a very high ascending limb in the first hour, becoming increasingly horizontal in the second and third hour. Here belong the ulcerative progressive cases with small cavities of the second stage and the unfavorable cases of the third stage. As a rule, the more the influence of the reaction is shifted from the third to the first hour in the sedimentation curve and the sharper the angle of the curve appears at the first hour, the more unfavorable the immune biological behavior of the particular case. Observations on the sedimentation curve after tuberculin stimulation did not succeed in the differentiation of active and nonactive cases. In a general way, the area of skin hypersensitiveness decreases when approaching the third stage, but this is not a rule, and small reactions (3 to 6 mm.) occur in normal controls as well as in cases of the second stage. During a general reaction the skin hypersensitiveness was increased, although later it slowly decreased with the treatment. There is a certain but not constant connection between skin hypersensitiveness and the lymphocytes. Formerly an increased white count was considered a sign of mixed infection, but now there is sufficient reason for the opinion that there can be an advanced pure tuberculosis with an increased white count. The blood picture within 24 hours after extract stimulation showed more or less leucocytosis with neutrophilia and lymphopenia, the Arneth-Schilling formula being shifted to the left. Some cases responded with a lymphocytosis. The sedimentation test is more sensitive to the specific stimulation than is the focal reaction, and is more adaptable in establishing certain rules concerning the reactions of the organism than is the skin hypersensitiveness, due to its greater independence of constitutional factors. The sedimentation test is as sensitive as the temperature. The differential leucocyte picture is more sensitive to specific stimulation than the temperature and the sedimentation test. The opinion of Fischel can be confirmed that the curve of sedimentation has more significance than the rate.—*The Effect of Specific Substances of Tubercle Bacilli on the Differential White Blood Picture. Skin Sensitiveness and the Rate of Sedimentation of the Red Cells, R. E. Flock and L. D. Scheff, Am. J. M. Sc., January, 1927, clxxiii, 59.—(U. E. Z.)*

Tuberculin Hypersensitiveness and Action.—Tuberculin hypersensitiveness is manifested by an increased inflammatory reacting power of the tissues. The reaction is not specific, since the same inflammatory response can be obtained by colon-dysentery bacilli. These nonspecific reaction foci flared up after the injection of old tuberculin. The histological picture resembled that of the tuberculin reaction. Attempts to produce tuberculin hypersensitiveness by preliminary treatment with dead tubercle bacilli resulted negatively. It is questioned whether tuberculin hypersensitiveness is a specific change, which can be caused only

by tuberculous infection. There are two possibilities: either an existing hypersensitiveness to a bacterial protein is increased by a tuberculous infection or a tuberculin hypersensitiveness occurs as a primary condition.—*Tuberkulinempfindlichkeit und Tuberkulinwirkung, H. Selter, Ztschr. f. Tuberk., 1926, xlv, 11.*—(*H. J. C.*)

Experimental Hypersensitiveness to Tuberculin.—Tuberculin, combined with guinea-pig or horse serum, as well as with Chamberland filtrates of tuberculous lungs, failed to sensitize guinea pigs. Tuberculin, added to the Chamberland filtrate of freshly prepared tuberculous organs of guinea pigs that had been killed two hours after the injection of old tuberculin, made guinea pigs sensitive.—*Zur Frage der Sensibilisierung gegen Tuberkulin, J. Caspari, Ztschr. f. Tuberk., 1926, xliv, 447.*—(*H. J. C.*)

Specificity of Tuberculin Reaction.—Nine normal guinea pigs, reacting negatively to tuberculin, were given two subcutaneous injections of *B. coli* vaccine. Sixteen to twenty days later 8 of them reacted strongly to intracutaneous injections of the colon vaccine, and 5 of them to tuberculin. Strong intracutaneous tuberculin reactions were still obtainable in these 5 guinea pigs one month later. In two of them the second tuberculin injection caused a reinflammation at the sites of previous injections of colon vaccine as well as tuberculin. The colon vaccine on second injection did not cause this lighting up at the site of previous reactions. Two tuberculous guinea pigs reacted both to tuberculin and colon vaccine. Histologically, no difference was noted between the colon and tuberculin papules in these animals.—*Zur Frage über die Spezifizität der Tuberkulinreaktion, M. Mastbaumt Ztschr. f. Immunitätsforsch. u. exper. Therap., October 15, 1926, xlviii, 428.*—(*E. R. L.*)

Effect of Adsorbents on Tuberculin.—The passage of several different lots of tuberculin through a Berkefeld filter resulted in the loss of potency of some of them, and led to a study of whether there was an adsorption of the active substances by the diatomaceous earth composing the filters. Experiments were made by using as adsorbents (1) powdered kieselguhr, (2) fuller's earth and (3) finely divided charcoal and tuberculins made both from glycerinated broth cultures and cultures grown on a synthetic medium: all were diluted with water, so that 200 cc. of the final product would contain 10 cc. of old tuberculin. These were crystal-clear, and separate portions of them were mixed with the different adsorbents and stirred frequently for 15 minutes, when the mixture was filtered through paper, the filtrates evaporated somewhat over a steam-bath, and used for testing hypersensitive animals along with "unadsorbed" portions of the preparations. The preparations thus treated showed a considerable loss of potency, the degree of loss depending upon the proportion between the bulk of tuberculin and the amount of the adsorbent. It would therefore appear that Berkefeld or Mandler filters will remove an appreciable amount of the active substances from tuberculin, at least when they are first used. When comparatively large quantities of strong tuberculin are filtered the loss is inappreciable or slight, but when a weak tuberculin, even in large amount, is filtered, it distinctly loses some of its potency. The adsorption is greater in tuberculin from synthetic media. Adsorbents, having a negative electrical charge, are much better than those (calcium carbonate) which carry a positive charge.—*Effect of Adsorbents upon Potency of Tuberculin, M. Dorset, R. R. Henley and H. E. Moskey, J. Am. Vet. Med. Assn., December, 1926, lxx (n.s. xxiii), 373.*—(*H. S. W.*)

Febrile Tuberculin Reaction.—The fever that follows the administration of tuberculin is supposed to depend upon the reaction at the focus of disease and to come from a specific irritation which liberates poisons from the focus that later irritate the heat centre in the brain. The latter may become allergic to such poisons. Experiments show that after tuberculous infection of rabbits, fever follows the introduction of tuberculin. But, if the local focus resulting from the inoculation be excised within the first three weeks of the infection, no febrile reaction occurs after the tuberculin. When, however, six weeks are allowed to elapse before excision, tuberculin will produce fever. There is no longer any tuberculosis even when excision of the focus has not occurred until six weeks after infection, and, although it is possible that a few bacilli may be in the lymphoid tissue without tubercle, they could exert no influence upon the fever. It therefore follows that the specific effect of tuberculin in producing fever is upon the heat centre that has been sensitized by virtue of the influence for six weeks of the tuberculosis upon that centre.—*Ueber die Abhängigkeit der Tuberkulinfieberreaktion vom tuberkulösen Herd, E. Toenniessen and H. Friederich, Deutsche Med. Wchnschr., November 19, 1926, lii, 1979.*—(*H. S. W.*)

Giant Cells in Intracutaneous Tuberculin Reaction.—From time to time, in retesting a tuberculous animal either intracutaneously or by other routes, an intracutaneous tuberculin reaction obtained several days previously may be observed to show an increase in erythema. This is usually designated as the "lighting-up of a previous site of reaction." No very satisfactory explanation of this interesting phenomenon has as yet been offered. Coca believes the pathological nature of the local tuberculin reaction to be that of tuberculosis, and that the specific character of the lesion may have some relation to the instances of a "lighting-up" at the site of previous injections after a subsequent one. Such a change is conceivably due to a mechanism similar to that which underlies the "focal reaction." In support of this theory, among others, Coca quotes Daels, who considers the tuberculin skin reaction to be of the nature of a local tubercle and believed it due to the presence of occasional killed bacilli and fragments of bacilli in tuberculin. Giant cells do develop in the previously reacting area, but Medlar sees in the giant cell of tuberculosis nothing more than a foreign-body giant cell. The authors examined histologically a number of intracutaneous tuberculin reactions produced by 10 per cent O. T. The early stages of the reaction are characterized by marked edema, fibrin deposit, exudate of polymorphonuclear leucocytes and eosinophiles, and necrosis of certain tissues. Necrosis of epithelium and fat cells occurs with great regularity. Sections from an early skin test show fat cells surrounded by a narrow zone of polymorphonuclear leucocytes, which are the cells that surround the fat during the stage of acute reaction. About these cells is a second zone consisting of endothelial leucocytes attracted by necrotic fat. A section made at a slightly later stage shows essentially the same condition, but the endothelial leucocytes surrounding fat and polymorphonuclear leucocytes have fused to form small foreign-body giant cells. In addition, larger giant cells are present, one of which is seen to contain fat droplets and partially surround a fat cell. Numerous fibroblasts are present. Later sections show the polymorphonuclear leucocytes gradually disappearing, and the resulting picture is that of giant cells surrounding fat or containing globules of fat. Still later all traces of fat may vanish, leaving giant cells embedded in dense fibrous stroma. Foreign-body giant cells have been seen to form about old fibrin and necrotic collagen. Necrosis of fat cells, however, is the chief exciting agent in their formation. If such an etiology is correct, then nonspecific necrosing agents may be expected to produce a similar result. Mallein in full strength (250 mgm. per cc.) produces in the skin of normal guinea pigs a reaction grossly similar to the intracutaneous tuberculin reaction, and in its later stages the microscopic picture in every way resembles that of the tuberculin reaction. Giant cells are formed in identical fashion. Consequently, there is nothing specific in the formation of these giant cells *per se.* That giant cells may form following necrosis of tissue in actual tuberculous lesions is an undoubted fact, but even there any specific character may be justly doubted (Medlar). The authors likewise regard them as nonspecific structures developing in response to necrosis and of no immunological significance.—*The Significance of Giant Cells in the Intradermal Tuberculin Reaction, F. W. Stewart and C. P. Rhoads, Am. J. Path., November, 1926, ii, 571.*—(*J. S. W.*)

Bacterial Lipoids in Production of Antilipoidal Sera.—The observations recorded in a previous paper lead to the question of whether the antigenic activity of alcoholic extracts from bacilli may not be due to an admixture of proteins. Rabbits were immunized with mixtures of alcoholic bacillary extracts and of the alcoholic extracts from horses' kidneys. They developed strong heterogenetic antisera. The production of such sera was not possible by the injection of any one of the two constituents alone. Since alcoholic extracts from tubercle bacilli and from proteus bacilli act as stimulants in the production of heterogenetic antibodies, the author concludes that they must contain proteins. The antisera produced by the mixtures react only with the organic lipoids and not with the bacillary lipoids.—*Über die Eignung von alkoholischen Bakterienextrakten zur immunisatorischen Entfaltung der Antigenfunktion von Lipoiden, A. Klopstock, Klin. Wchnschr., January 15, 1927, vi, 120.*—(*M. P.*)

Antigenic Function of Bacterial Lipoids.—Animals immunized with whole tubercle bacilli develop humoral antibodes, which react with the whole bacilli and with alcoholic bacillary extracts. These antisera not only contain specific antibodies against the bacilli lipoids, but they also react with alcohol-soluble lipoids from animal organs. Rabbits, which were immunized with bacillus proteus *X19*, produced antibodies against these bacilli, but no lipoidal antibodies. Rabbits immunized with alcoholic extracts from proteus *X19* produced antibodies which reacted with various nonspecific

lipoids in a similar way as Wassermann positive sera. Antisera, produced by the injection of alcoholic tubercle-bacillus extracts, reacted similarly to alcoholic proteus extracts. The behavior of the bacterial lipoids is different immunologically from that of organic lipoids, inasmuch as they produce antibodies without the addition of a serum, which is necessary for the production of lipoidal antibodies produced by organic lipoids.—*Zur Kenntnis der Antigenfunktion von Bakterienlipoiden, A. Klopstock and E. Witebsky, Klin. Wchnschr., January 15, 1927, vi, 119.*—(*M. P.*)

Antibodies and Antigen in Blood and Pleural Fluids.—The exudates, occurring with pleuritis and during the course of artificial-pneumothorax therapy, contain the same quantity of antibodies as does the blood-serum. The fluid of pleurisy with effusion is, however, totally lacking in antigen, while that occurring in pneumothorax cases has at times marked antigenic properties.—*Recherche comparative des anticorps et de l'antigène tuberculeux dans le sang et les liquides pleuraux, Salomon and J. Valtis, Meeting, Soc. de Biologie de Paris, November 7, 1925, reported in Presse Méd., November 18, 1925, no. 92, 1527.*—(*E. H. K.*)

Immunity Experiments with Dead Tubercle Bacilli.—The allergic state can be set up in guinea pigs after several injections of heat-killed tubercle bacilli. Experiments were done to determine whether the allergy induced by killed bacilli would result in an increased resistance against subsequent infection with living bacilli, and whether it ran parallel in degree with the intensity of the tuberculin allergy. The latter question is not particularly emphasized in the work reported. The maximum skin test with 5 per cent old tuberculin in the sensitized animal ranged from 10 x 10 mm. to 25 x 25 mm., except in the animals injected with defatted bacilli, which gave rather poor skin tests. A high mortality from intercurrent disease was encountered, as is usually the case in experiments of this nature in which the animals must be observed for many months. No animals dying of intercurrent disease within fifty days of the introduction of the infecting material are reported in the series, and this ruling applied to immunized and control animals alike. The test animals were sensitized by intraperitoneal injections of dried heat-killed (100°C. for one hour) tubercle bacilli (H 37, human origin), with the exception of a small group which received Dreyer's defatted bacilli subcutaneously. The intraperitoneal dose ranged from 2 to 5 mgm., and it was finally concluded that three injections of 2.5 mgm., four days apart, making a total of 7.5 mgm., conferred the best allergic state, as demonstrated by the tuberculin intracutaneous test. Only tuberculin-negative guinea pigs, weighing at least 400 gm., were used in the experiments. Three weeks after sensitization the skin test was again performed to determine the degree of allergy present. The same strain of tubercle bacilli (H 37) was used for infecting the animals, in doses ranging from 0.002 to 0.004 mgm. of bacilli, dry weight, in a suspension as free from clumps as possible. The inoculation was made subcutaneously in the inguinal region, except when the orbital route was selected. In selecting the control animals the attempt was made to use guinea pigs of the same weight and age as those of the sensitized animals or as near these as possible. Infection was not done until a high degree of allergy was present in the test guinea pigs of each series. *Series I:* Fourteen guinea pigs, with an equal number of controls, are included in the series. The sensitized animals outlived the controls, the average length of life in the former being 208 days, and in the latter 146 days. There was more extensive disease in the controls than in the sensitized animals. *Series II:* This group received the maximum dose of killed bacilli, 15 mgm., and consisted of 24 animals in all, 12 test and 12 control. Beginning on the sixty-second day after the infecting dose, 8 of the animals were killed in groups of 2 test animals and 2 controls. Much less tuberculosis was found in the test animals than in the controls. Among the remaining guinea pigs, the test animals long outlived the controls in every instance. *Series III:* This series gave similar results. The average length of life in the sensitized animals was 229 days, and in the controls 166 days. *Series IV:* In this group there were 132 guinea pigs both sensitized and controls. After infection (0.002 mgm.) the series was further divided into two groups, one of which received no further treatment, while the other was treated with dead bacilli in three doses totaling 2.5 mgm. In the untreated group the sensitized guinea pigs averaged 171 days of life while the controls averaged 150. In the treated group, the average days of life were 148 for the sensitized pigs and 120 for the controls. If the two series are compared it will be seen that the further introduction of killed bacilli plays no further part in the mechanism of resistance. *Eye Experiments:* Two small series of sensitized guinea pigs, together with their controls, received 0.004 mgm. of living tubercle bacilli by inoculation through the lens into the

vitreous humor. A reaction always appeared twenty-four hours after the inoculation in the sensitized animals. The results obtained were similar to those reported for the other series. *Dreyer's Defatted Bacilli:* A small series was sensitized with these bacilli by both subcutaneous and intraperitoneal injections. Together with the necessary controls all were injected with from 0.001 to 0.002 mgm. of live bacilli. The average length of life in the test guinea pigs was 135 days and in the controls 123. Defatted bacilli do not appear to confer any appreciable protection in guinea pigs. In all the above experiments many animals were lost from intercurrent disease. The microörganism responsible was found to be Friedländer's bacillus, and the pneumonia never occurred in epidemic form nor was there a seasonal variation. However, when there was an extensive progressive tuberculosis, pneumonia did not occur. Most of the animals died during the preallergic or during the sensitization period. Out of more than 400 guinea pigs used in the various experiments, there were only 97 sensitized and 96 controls that could be utilized with certainty. The method of infection was not very accurate, due to spontaneous agglutination or clumping of bacilli. It is probable that the lack of uniform disease in guinea pigs is due not so much to the individual resistance of the animals, as to the clumps which are present in a suspension of living tubercle bacilli on inoculation, a fact which very likely influences the dissemination of the microorganisms. It is now believed that the infecting dose used was too large. *Conclusions:* Guinea pigs sensitized with dead tubercle bacilli and subsequently inoculated with living bacilli outlived the controls on average of 46 days. The amount of macroscopic disease at autopsy in the former was much less extensive than in the latter, confirming the belief that dead bacilli can induce some degree of protection. Dreyer's defatted bacilli produces no appreciable resistance in guinea pigs.—*Immunological Studies in Tuberculosis. IV. Concerning the Resistance to Infection of Animals Sensitized with Killed Bacilli, S. A. Petroff and F. W. Stewart, J. Immunol., August, 1926, xii, 97.*—(*J. S. W.*)

Serological Relationships of Acid-fast Bacilli.—Attempts to differentiate various acid-fast bacilli by means of agglutination tests have failed, whereas the complement-fixation test has revealed a universally strong group reaction. It has been found that the antigenic property of acid-fast bacteria tested with tuberculous sera diminishes in a scale represented by mammalian bacilli at one end and saprophytic microörganisms at the other. The author has attempted to analyze the antigenic relationship of various races of acid-fast bacilli by means of complement-fixation tests, agglutination, and absorption experiments. The studies made indicate that types cannot be established on a purely serological basis, since none of the types except the mammalian appears to be homogeneous. For agglutination fine suspensions of living bacillary bodies were used. For complement-fixation tests the same suspensions were heated to from 60 to 65°C. for forty minutes. The immune sera were obtained by means of repeated intravenous inoculations of rabbits with suspensions heated in the same way. Rabbits, immunized against human tubercle bacilli, received a preliminary intraperitoneal inoculation of 0.1 mgm. of living human culture; rabbits immunized against bovine tubercle bacilli receive a preliminary subcutaneous injection of 0.001 mgm. of the living bovine culture. The quantity of complement used was from 0.15 to 0.20 cc. diluted 1:10. One-third of the maximum nonanticomplementary dose of antigen was employed, and the incubation period in the preliminary, as well as in the main experiment, was ninety minutes. *Conclusions:* There are qualitative differences in the antigenic structure of various acid-fast bacilli. These differences cannot be demonstrated clearly by the direct agglutination tests because of the complete or partial inagglutinability of most of the acid-fast bacilli. The presence of agglutinins in immune sera may be detected only if one is fortunate enough to find an agglutinable strain of the same or related type. Since inagglutinable strains produce agglutinins for agglutinable strains, and are able to absorb the produced agglutinins, it is obvious that they possess agglutinogens; but we have no definite index of the amount of agglutinins present in their immune sera. Complement-fixation and absorption experiments can be successfully applied to the antigenic analysis of this group of microörganisms. Inagglutinability of acid-fast bacilli is doubtless due in part to a physicochemical interference with flocculation, but it is probable that all receptors detectable by complement fixation are not involved in the formation of flocculi. Mammalian tubercle bacilli have an antigenic structure different from all other acid-fast bacilli. No differentiation within the mammalian group has thus far been found possible. One atypical bovine strain is an exception to this statement. Avian tubercle bacilli likewise differ qualitatively

from all other microörganisms, but do not form a homogeneous group for there are at least three avian subtypes. The nonchromogenic strains isolated from patients with leprosy by Kedrowsky and by Duval and the agglutinable culture of Arloing belong in this group. A serologically distinguishable group of acid-fast bacilli from cold-blooded animals does not exist. In antigenic structure these microörganisms show very little similarity to one another and to other acid-fast bacilli. Acid-fast saprophytes differ qualitatively from all other acid-fast bacteria. Within the saprophytic acid-fast group there is at least one fixed subtype, for strains from various sources, such as those designated "smegma," "mist," "milk," "pseudo-tuberculosis," and "Butter R," have been found to be closely related if not identical. These observations disprove the hypothesis that acid-fast bacilli possess a common antigen present in varying proportions in various strains, but show that qualitative differences occur, and suggest the possibility that serological methods may be used to identify acid-fast microörganisms.—*On the Serological Relationship of Acid-fast Bacteria, J. Furth, J. Immunol., October, 1926, xii, 273.—(J. S. W.)*

Mutation Forms of Tubercle Bacillus.—After a certain time of exposure of apparently pure cultures of tubercle bacilli to sanocrysin, various forms appeared which were not acid-fast. They were gram-negative, motile, and grew rapidly. A peculiar pathological change occurred following their injection into guinea pigs. They were at first regarded as contaminations, but the same result was obtained with other cultures. These same unusual forms were also obtained by grinding the germs for six to eighteen hours in a ball-mill and planting the residue in dextrose-bouillon. They were also planted on media unfavorable for growth, such as inulin, dulcite and mannite bouillons, with the same result. Cultures from other laboratories were similarly studied and the peculiar forms were again obtained. A specially purified culture of fresh microörganisms can be made to produce bacillary forms (diphtheroids and solids) and coccoid forms (diplococci and tetrads) that are not acid-fast and do not produce typical tuberculous disease after one passage. It is very probable that many tetrad forms found in tuberculous lesions are mutants of the tubercle bacillus. Most of these tetrad forms have been found in tuberculous cavities and sinuses. These studies lend support to the theory of Fraenkel and Much that Hodgkin's disease arises from tuberculosis. It is possible also that other lesions such as polyserositis and Pick's cirrhosis may be caused by such microorganisms. Artificial mediums and the long continued variations in temperature, oxygen and moisture develop easily changeable forms, although more stable fresh cultures can be altered. Karwacki suggests that lipases and antibodies are responsible for these variations. It is common to see tubercle bacilli, suspended in certain pleural exudates, become nonacid-fast, granular and coccoidal. There is reason to believe that the classical acid-fast form of bacillus is not the only cause of pathological changes in tuberculosis and its complications. *Conclusions:* 1. In a study of various conditions under which mutation forms of the tubercle bacillus may develop, it is found that mutation takes place with regularity during vegetation, depending on the fundamental law of variation together with a particular alteration of environment. 2. A constant favorable environment is difficult to maintain for a long period either in old cultures or lesions. In either instance split forms may appear that are vastly different from the tubercle bacillus. 3. Accordingly, there are produced mutation forms that may assume a great variety of cultural, morphological and pathological characteristics. 4. The two most common types of mutants are the bacillary and the coccoidal forms, although filter-passing forms also appear to exist. 5. Bacillary forms may pass over into coccoid forms, and granules and coccoidal forms may grow into bacilli if the medium is suitable. 6. The mutation forms appear to develop from some of the gram-positive granules which are perhaps resting stages of tubercle bacilli. When cocci are formed there is a tendency to develop first diplococci, and later various tetrads and staphylococcus-like forms may develop. Bacillary forms also may develop. 7. Many of these mutants are not pathogenic. Many are of low pathogenicity, while others undoubtedly play a definite rôle in disease processes. 8. The suggestion is offered that certain chronic diseases (like Hodgkin's disease and polyserositis) may be caused by mutation forms of tubercle bacilli.—*Mutation Forms of the Tubercle Bacillus, H. C. Sweany, J. Am. M. Ass., October 9, 1926, lxxxvii, 1206.—(U. E. Z.)*

Transmutation of Saprophytic into Pathogenic Acid-Fast Bacilli.—Attempts were made to transform acid-fast saprophytes, Timothy bacilli, butter bacilli of Rabinowitsch, and Smegma bacilli, into genuine tubercle bacilli by cultivating them on lactic acid (Much) 1:10,000, on vitamine-free media (Setti), and on bouillon containing

1 to 2 per cent old tuberculin, and by diminishing the resistance of guinea pigs by means of starvation or vitamine-free diets, and then injecting them with these bacilli. The lactic-acid strains revealed no definite virulence, but in three guinea pigs there was an increase of virulence in that the microorganisms flourished in the animals yet produced no toxemia. The vitamine-free strains exhibited the change in virulence in less distinct form. All other attempts proved negative. It is concluded that the question of the transmutation of saprophytic forms to tubercle bacilli still remains open.—*Untersuchungen über die Möglichkeit eines Überganges von säurefesten Saprophyten in echte Tuberkelbacillen, S. Zlatogoroff, M. Zechnowitzer and M. Koschkin, Ztschr. f. Hyg., 1926, cv, 583.*—(*H. J. C.*)

Method for Counting Tubercle Bacilli.—In preparing suspensions of living tubercle bacilli for animal inoculation, in which a numerically accurate dose is required, three outstanding difficulties are encountered: that of obtaining a suspension free from clumps, of preventing spontaneous agglutination on standing, and of counting accurately the number of microörganisms in a unit volume of the suspension. The method presented aims to overcome these difficulties and to avoid, at the same time, undue manipulation and exposure. Spontaneous agglutination was found not to take place between pH 8 and pH 9, and did not occur on standing. N/15 Na_2HPO_4 proved a satisfactory solution for preparing suspensions as it is isotonic, with a hydrogen ion concentration of about 8.7. To prepare a suspension free from clumps and extraneous material it is necessary to filter through paper. The bacilli, grown on broth, are blotted and ground in a mortar, in the usual way, with N/15 Na_2HPO_4 solution. The suspension is then diluted in a test tube until the outline of a pencil held against the tube becomes distinct; in other words, to about the concentration of an agglutinating suspension. The suspension is now immediately filtered twice through two sheets of Whatman paper No. 5, which have been previously thoroughly washed with distilled water to get rid of dust, shreds, etc. The resulting filtrate, after this procedure is practically free from any foreign material and usually only single microörganisms are present. If clumps of three or more are found the suspension is discarded. It is not necessary to obtain a particularly fine suspension before filtering, but merely to have a reasonable number of discrete bacilli. Apparently a certain number of clumps are necessary to block some of the larger spaces in the paper so that only single bacteria may pass on second filtration. For counting, a Levy-Hausser counting chamber, ground in one piece and 0.02 mm. deep, is used, with an 0.18 mm. reinforced cover-slip. A high dry lens, magnifying 580 diameters, makes it very easy to distinguish the bacilli providing the lighting system is altered. If the Abbe condenser is removed and replaced with a center-stop 1 or 2 mm. in diameter, the bacilli stand out plainly and can be readily differentiated from foreign particles. A suspension counted by this method and showing 3,700,000 bacilli per cc., after standing at room temperature for three hours, gave a count of 3,600,000. The suspension was not shaken. Finally, the suspension was diluted with the phosphate solution, so that 0.5 cc. contained 5, 10, 25, 50 and 100 bacilli. One-half cubic centimetre amounts were injected subcutaneously into the groin of a series of guinea pigs. Practically all animals receiving more than 10 bacilli became sensitive to tuberculin, as well as the majority of those receiving a smaller dose than this. The method described is important in the fact that a precise study of experimental tuberculosis can now be undertaken, with the assurance that the infecting doses, given to the smaller laboratory animals, will be uniform. In the past, methods for determining and controlling the dosages have been inadequate and experiments in tuberculosis immunity were consequently hampered.—*A New Method for Suspending and Counting Living Tubercle Bacilli, F. B. Jennings, Jr., J. Infect. Dis., October, 1926, xxxix, 310.*—(*J. S. W.*)

Filtrates of Tuberculous Materials Not Infectious.—An attempt to cultivate tubercle bacilli of typical forms, according to Vaudremer, from the filtrates of ordinary tubercle-bacillus cultures (human, bovine and avian types, grown on glycerine-potato, egg or glycerine-bouillion) or from material containing tubercle bacilli (caseated tuberculous lymph nodes from guinea pigs and rabbits, and the kidney from a tuberculosis patient) resulted entirely negatively. It was not possible to cause tuberculous changes in guinea pigs and rabbits by the inoculation of these filtrates, nor to produce an allergy to tuberculin.—*Filtrationsversuche an Tuberkelbacillen, A. Fessler, Centralbl. f. Bakt., 1926, xcviii, 148.*—(*H. J. C.*)

Survival of Tubercle Bacillus in Physiological Salt Solution.—The length of time that tubercle bacilli will live and maintain virulence when suspended in physiological salt solution has never been determined. This note is to place on record the observa-

tion that the germs were alive and virulent for guinea pigs in three suspensions of tubercle bacilli in physiological saline solution which had been stored for periods of three hundred and ten, three hundred and twenty-five and three hundred and thirty days respectively, at refrigerator temperature. The refrigerator fluctuated about the freezing point, the fluctuation not being recorded. The suspensions were made by lightly grinding the moist bacilli from active glycerol-agar cultures in an agate mortar, adding 0.85 per cent sodium chloride solution slowly at first and then more rapidly to the amount of 1 cc. per milligram of bacilli. The suspensions were stored in narrow-neck, round flasks of pyrex glass stoppered with cotton. Evaporation was not measured, but it was slight. Two of these suspensions were bovine and the other was human. Two guinea pigs were used, one receiving 0.1 mgm. of bacilli intraperitoneally and the other 1 mgm. in like manner. All these animals developed a well-marked generalized tuberculosis, and there was nothing atypical in the course of the disease or in the autopsy findings.—*The Survival of the Tubercle Bacillus in Physiological Salt Solution, E. Shope, J. Exper. Med., November 1, 1926, xliv, 623.—(J. S. W.)*

Action of Metallic Salts on Growth of Tubercle Bacilli.—Metallic salts, particularly of manganese, copper, silver, gold and platinum favor the growth of stock cultures of bacteria. While the growth of old laboratory strains of the tubercle bacillus is stimulated by this means, the isolation of new cultures on the Petroff medium is not facilitated, nor is the latent period shortened by the addition of metallic salts. The bovine type of tubercle bacillus often grows poorly on the Petroff medium, but the addition of metallic salts in certain concentrations hastens it.—*Die fördernde Wirkung einiger Metallsalze auf das Bakterienwachstum im besonderen Hinblick auf die Züchtung von Tuberkelbazillen, K. A. Jensen, Ztschr. f. Immunitätsforsch. u. exper. Therap., January 26, 1926, xlvi, 59.—(E. R. L.)*

Menstrual Fever in Pulmonary Tuberculosis.—Among the numerous factors provoking febrile manifestations in pulmonary tuberculosis, menstruation has long been recognized. All phthisiologists have observed the transformation of the pulmonary signs at the catamenial period. There has not, however, appeared a complete and comprehensive study of the clinical facts and their pathological interpretation. Many of the older authors remarked on the frequent appearance of unfavorable symptoms at this time and on the predisposition to congestive attacks. There have also been noted postmenstrual aggravations. There seems to be a tendency to increased pulmonary exudation associated with the menses and their vasomotor reactions. The possibility of the occurrence at this time of true bacillary septicemias must be borne in mind. A definite distinction is drawn between premenstrual, menstrual and postmenstrual reactions. *Premenstrual fever* is defined as elevation of rectal temperature beginning eight, ten, or even fifteen days before the first day of the menses. *Menstrual fever* is defined as that beginning the day before or the first day of the flow and generally terminating with it. *Consecutive or postmenstrual* fever is that which occurs in the days following the end of the menstrual period. *1: Menstrual Variations of Temperature in Normal Women:* Normally there is never elevation of temperature during the menses, although a slight premenstrual rise is the rule. On the contrary, a lowered body temperature is generally observed. This slight fluctuation is observed in two-thirds of normal women, while a minority show no effect whatsoever on body temperature. *2: Premenstrual and Menstrual Variations of Temperature in Women with Pulmonary Tuberculosis:* In these the degree of premenstrual rise is apt to be exaggerated. Summarizing, one can say that women with pulmonary tuberculosis, according to the degree of activity of their lesions, present, at the occasion of their menses, thermic reactions which may be either an exaggeration of the normal or completely abnormal. Quiescent or inactive tuberculosis has no effect on the normal course of affairs. *3: Menstrual Temperature Curves in Normally Menstruating Tuberculous Women:* No menstrual modification of the temperature curve was noted in 16 per cent of 400 menstrual periods studied. Premenstrual fever of some type other than normal was noted in 0.5 per cent. However, menstrual hypothermia occurred in 28 per cent. Neither premenstrual nor postmenstrual hypothermia was noted. Menstrual fever (hyperthermia) occurred in 32 per cent, or twice the proportion in whom reactions of the normal type were noted. Menstrual fever may take one of three forms: (1) increase in amplitude of the thermic oscillations (12 per cent), (2) steeple-like hyperthermia during the periods (10 per cent), and (3) elevation of the mean temperature level (10 per cent). *a: Increase in Amplitude of Thermic Oscillations:* At times this amplitude reaches a maximum of 1 to 1.2°C., although ordinarily much less. *b: Steeple-like Menstrual Hyperthermia:* This may

reach from 0.4 to 0.6°C. above the ordinary maximum. It usually occurs toward the middle or latter part of the period. Occasionally there are two such elevations. *c: Elevation of Mean Temperature Level:* In this case both maximum and minimum temperatures are raised, beginning with the onset of menstruation. There is also seen (*d*) *abrupt steeple-like hyperthermia just before the menses.* This occurs in 11 per cent of cases. *4: Study of Thermic Curves in Nonmenstruating Tuberculous Women:* A distinction is made between "active amenorrhea," in which the flow is lacking, but there are observed all the general nervous, psychic and thermal phenomena, as well as the local signs, lumbar pains, sense of weight, etc., and "silent amenorrhea," in which there is neither flow nor local reactions. The woman seems as though castrated; she "forgets her sex." In active amenorrhea we have, at the usual date of menstruation, all the phenomena, normal and abnormal, previously described, and the intensity of the reaction is proportional to the evolutive character of the lesions. In silent amenorrhea we have a dead genital system in an already decayed organism; it is a cachectic state. In other cases the genital system is not dead but dormant, and often associated with a subfebrile temperature. *5: Thermic Menstrual Curve in Dysmenorrheic Tuberculous Women:* When menstruation returns after being absent, the first period commonly assumes the normal type and a lowering of the temperature is common. There appears to be no appreciable relation between the menstrual reaction and irregularity, duration or frequency of the periods. *6: Postmenstrual Thermic Reactions:* These often correspond with a frank aggravation of the disease, sometimes of extreme gravity. Postmenstrual febrile reactions were found to occur in 12 per cent of cases. In 7 per cent the reactions were termed "benign," including steeple-like hyperthermia, 1 per cent, elevation of the mean temperature level, 3 per cent, and increased amplitude of oscillations, 3 per cent. In artificial-pneumothorax cases, such a benign postmortem thermic reaction may signalize the appearance of an effusion. The "grave" postmenstrual thermic reactions usually usher in pneumonia and miliary processes, or a terminal meningitis. Three typical cases are cited. In certain cases distant complications, renal, meningeal or peritoneal, develop, in others new pulmonary foci. *7: Prognostic Value of Menstrual Fever:* The clinical studies just cited allow certain important deductions as to the relation between menstrual and postmenstrual reactions and activity or nonactivity of pulmonary lesions. Two cases are cited, the first illustrating menstrual reactions with progressive aggravation of the disease, the other menstrual reactions with progressive amelioration, the reactions gradually lessening and finally giving way to the normal menstrual hypothermia. The gravest reactions are of the type with increased amplitude of oscillations or else elevation of the mean temperature level. A knowledge of the significance of the various menstrual reactions is of great value in prescribing the proper measures, including the conduct of pneumothorax cases. The steeple-like ascensions seem to be of least serious significance. They are only warnings, while the other types are "tolling bells." The following conclusions, which are almost laws, are deduced: *1: Lesion quiescent, not active,* with or without induced pneumothorax,—normal menstrual reaction, that is, premenstrual fever with hypothermia during the flow. *2: Active lesion:* increased amplitude of thermic oscillations; elevation of mean temperature level during the flow; often a consecutive or postmenstrual thermic reaction. *3: Transition* between a period of amelioration and aggravation or the reverse,—steeple-like hyperthermia during the menstrual flow. *Pathogenic Study: 1: Rôle of Infectious Diseases:* Ordinarily during convalescence from most infectious diseases the normal type of menstrual reaction occurs, and menstrual hyperthermia seems truly to be confined to certain types of pulmonary tuberculosis. One cannot postulate lesions in the genital tract to account for it, as both clinical and necropsy evidence is opposed. The cause cannot, therefore, be attributed to local infection. *2: Toxic Theory:* Long ago the premenstrual period in the female was thought to correspond with a physiological accumulation of toxic substances which the menses eliminated. But it is less easy to explain menstrual hyperthermia in grave cases. It is true that some authors postulate toxic substances in the blood-serum, but there is no explanation of why these are normally eliminated but not so in grave tuberculosis. On the other hand, Caussimon has determined the fact that blood-serum of a woman in the menstrual hypothermia state lowers the temperature of a normal guinea pig, while blood-serum in the premenstrual hyperthermia state raises it. However, we are still at sea on the nature of the hyperthermic principle, although variations in endocrine activity are now postulated as the active cause. *3: Vasomotor and Nervous Theories:* In every patient the pulmonary signs are affected several days before the periods, and there is evidence of abnormal

exudation in the pulmonary parenchyma, transitory in patients who are doing well but often persistent in those progressing unfavorably. The following facts are deduced: (1) pulmonary vasodilatation is associated with thermic menstrual reactions; (2) before and during the flow the rectal and axillary temperatures seem to vary inversely, corresponding to visceral and peripheral vasomotor changes; (3) there are two stages in the menstrual thermic reactions: the first, a premenstrual hyperthermia, corresponding to visceral vasodilatation; the second, menstrual hypothermia, to thoraco-abdominal vasoconstriction, which checks the pelvic vasodilatation; (4) in thermic reactions of abnormal type these vasomotor reactions appear to be disturbed. Those vasomotor reactions are, of course, governed by the nervous system, the thermoregulatory centres being reflexly excited. Caussimon, differing from Daremberg, regards the time of onset of pulmonary vasoconstriction as a time of elevated pulmonary arterial blood-pressure, while the aortic pressure is lowered. Studies of arterial pressure show hypertension preceding the flow and followed by hypotension. The conception is held that in the premenstrual period, when visceral vasodilatation is taking place, arterial tension is lowered and there is hyperthermia; at the moment when the flow begins there is a reflex pulmonary vasoconstriction with increased pulmonary arterial pressure and lowered left auricular pressure. Aortic pressure undergoes a transitory elevation, followed by a depression. F. Franck says that the uterus plays the part of a stopcock on the arm of an elastic tube. During this phase of hypotension central temperature falls. The rôle of the sympathetic and vagus nerves and the significance of the oculocardiac reflex are discussed. *4: Endocrine Theory:* Ovulation precedes menstruation by six to ten days and the maturation of the corpus luteum corresponds with the onset of the menses. We know that this maturation goes on in "active amenorrhea." Corpus-luteum extract is found to exert a hypotensive influence, as is also ovarian extract. Others have described a vasodilator effect and a hyperthermic effect. The corpus luteum also probably stimulates thyroid activity which is known to excite fever. *5: Rôle of Tuberculous Bacillemia:* It is evident that physiological mechanisms alone do not suffice to explain all the facts and that the tuberculous process and its activity must be considered. Congestion about tuberculous lesion is known to favor dissemination and propagation. In fact, the tubercle bacillus has been demonstrated in the circulating blood at menstruation in a number of cases (10 out of 34) and all of these showed definitely abnormal febrile reactions. Guinea-pig inoculation was also performed, but fewer positive results were obtained (19 per cent). The tubercle bacillus, in recent lesions, is separated from the blood by only a thin, more or less fragile, histological barrier, which may be passed during a violent congestion. Associated phenomena are enlarged liver, coated tongue, digestive disturbance, and often diarrhea. It is thought that such attacks of bacillary septicemia play an important rôle in the formation of new foci, both pleural and extrapulmonary, as well as pulmonary. Thus, from the character of the menstrual reactions we can deduce the state of encapsulation or arrest of the pulmonary lesion.—*Les fièvres menstruelles dans la tuberculose pulmonaire, E. Leuret and J. Caussimon, Rev. d. l. Tuberc., December, 1925, vi, 689.—(A. P.)*

Habitual Hyperthermia.—Habitual hyperthermia can only be considered such in cases in which a subfebrile or febrile fever curve, not only by rectal but also by axillary determination, occurs for weeks or months. In order to assure the diagnosis every possibility of the presence of an organic disease must be excluded by repeated exhaustive diagnostic tests. The organs of hearing, nose and throat should not be neglected, and a careful examination of the urine and blood should be made. To determine an occult tuberculous focus a one-hour walk should be prescribed and the temperature reactions to this carefully studied; and, if no deviation from normal occurs, a subcutaneous tuberculin test of 10 mgm. O. T. should be made. Habitual hyperthermia is regarded as a general symptom of a neurosis in a psychically below-par individual The condition is very rare.—*Über habituelle Hyperthermie, K. Brünecke, Beitr. z. Klin. d. Tuberk., 1926, lxiii, 412.—(H. J. C.)*

Afebrile Tachycardia in Early Pulmonary Tuberculosis.—Attention is drawn to the practical importance and frequent occurrence in adults of long continued afebrile tachycardia as a sign of activity in early phthisis. To be classified as early, individual cases should not present extensive physical signs, cardiac disease or other displacements, or marked constitutional disturbances. The lowest pulse-rates, persisting for a week or so at a time when all other prognostic criteria are favorable, are assumed as normal in the several cases given as illustrations. A normal diurnal variation in the pulse-rate is recog-

nized. Two clinical types of rapid pulse have been noted: (1) the swinging type, which is either an exaggeration of the normal diurnal variation, or else an increased rate throughout, with a daily swing of about 85 to 110; and (2) the irregular type, in which there is no regular daily variation but the pulse holds to a rough average of 90–100. These types may both occur in the same individual at different stages of his treatment. The morning rate is the more important and represents the basic rate, and the evening pulse discloses the degree of irritability. Tachycardia marks the rise and fall of a toxemic wave, and can generally be associated with a toxic crisis, such as hemoptysis or an attack of pleurisy. Its occurrence in all cases of early uncomplicated phthisis may wisely be considered as a manifestation of activity until satisfactory evidence to the contrary is obtained. No cases should be thought of as quiescent as long as this symptom exists, even though the clinical course has been entirely apyrexial. There is need for a more detailed observation of the pulse-rate during the course of early pulmonary tuberculosis.—*Afebrile Tachycardia in Early Phthisis, R. Delmege, Lancet, October 30, 1926, ccxi, 899.—(R. S. A.)*

Nontuberculous Hemoptysis.—The bleeding, often attributed to hemoptysis of tuberculous origin, may come from the pharynx, larynx, trachea, bronchi or lungs, independently of tuberculous lesions. Laryngeal and tracheal hemorrhages are very rare. Thermal and chemical agents may provoke bleeding by their irritant action on the mucous membrane of the respiratory system. Gas, acids and occasionally ether, belong to this class. Violent coughing may cause small hemorrhages, especially in individuals whose vascular structure is fragile and who have a tendency toward the formation of venous varices. Other causes of bronchial hemorrhages are chronic inflammatory processes, bronchiectasis, and putrid bronchitis. Congestive lesions in the lung may cause hemorrhagic expectoration. Abscess, gangrene, and more rarely malignancy and syphilis, are other possible factors. In certain localities parasitic diseases of the lung give rise to serious hemoptyses. In Italy the echinococcus is often encountered. In Japan and China several parasites have been described as etiological agents in pulmonary hemorrhages. Some of these are the diastoma westermanni, pulmonary distomiasis of Boelz, and pulmonary gregarinosis. Lesions of the mitral valve, especially stenosis, very frequently induce dangerous hemoptyses. Hemophilia and aortic aneurysm are rare causes of bleeding from the lungs. According to some authors, there are certain pulmonary hemorrhages, due to lesions (organic or functional) of the nervous system. Hemoptysis has been described in cases of hysteria, chorea and epilepsy, and in nontuberculous lesions of the spinal medulla and brain. Hysteria should very cautiously, if ever, be given as a possible cause. Pulmonary bleeding at the time of the menstrual flow is very often seen. This vicarious menstruation is believed by some authors to arise as a reflex from the genital system through the sympathetic chain, which controls vasomotor equilibrium. Tuberculosis, however, is the cause of over 60 per cent of hemoptyses.—*Le emottisi non tubercolari, G. Milani, Tubercolosi, August, 1926, xviii, 253.—(U. E. Z.)*

Nontuberculous Hemoptysis.—Since hemoptysis is so commonly a symptom which introduces tuberculosis, there is no wonder that the diagnosis of tuberculosis from this symptom should be incorrect at times. The pulmonary diseases that may cause hemoptysis are numerous, such as fibrinous bronchitis, influenza, pneumonia, bronchiectasis, leukemic foci of the lung, pulmonary abscess, gangrene, tumors, mycoses, syphilis, etc. However, examination of sputum and the roentgenograph will usually quickly clear up the diagnosis. Pulmonary bleeding from cardiac disease is quite different, and there is an increasing number of cardiac cases diagnosed as tuberculosis. Many of these are sent to tuberculosis sanatoria, where they ordinarily do well. Streaked sputum from cardiac disease may come from two sources, namely, emboli and chronic passive congestion. In the latter the marked dyspnea and widespread pulmonary changes, râles, etc., and the finding of heart-failure cells in the sputum should point to the proper diagnosis. Emboli come usually from a phlebitis or cardiac thrombi. The source of the former are usually easy to determine. But the small bits of thrombi which plug only the smaller vessels usually give no clinical or roentgenological sign of their presence. The X-ray appearance from the infarcted areas set up by larger emboli at times quite resemble a small patch of tuberculosis. The collateral bronchial inflammation that is usually associated with them may also suggest tuberculosis. Such sources of error are a good deal more frequent than we realize and should always be borne in mind. The absence of tubercle bacilli and the presence of heart-failure cells in the sputum and, of greatest importance, signs or symptoms of mitral or other cardiac disease, will

usually correct the mistaken diagnosis.—*Nichttuberkulöse Lungenblutungen, A. Hoffmann, Deutsche med. Wchnschr., September 17, 1926, lii, 1581.—(H. S. W.)*

Blood Pressure in Pulmonary Tuberculosis.—Blood-pressure studies were made on a group of 701 tuberculous patients, free from cardiorenal and metabolic disturbances. The systolic reading was taken when the first sound was heard and the diastolic pressure was recorded when all sounds ceased. Blood-pressures were taken every four to six weeks. The estimations were made with the patients seated and approximately three hours after meals. The mean blood-pressure in patients of the 41–50 age-group, with the disease in stage II, is lower than that of a similar group with stage-III disease. This is probably due to the large number of fibroid cases in the stage-III group. Increase of blood-pressure with age in all stages is quite apparent. The mean diastolic pressure in the majority of cases increases with advancing age, the most marked advance being noted in incipient cases. The increase in pulse-pressure is noted particularly in female patients over forty years of age. The diastolic pressure is not much lowered in patients with active disease, but the pulse-pressure is distinctly diminished in active cases, particularly in advanced age-groups. In earlier years the diagnostic criteria of incipient as well as of advanced tuberculosis included low blood-pressure. Many individuals with non-tuberculous pulmonary complaints, classed as neurocirculatory asthenics, presented blood pressures identical to those found in patients with minimal tuberculosis. Many of these nontuberculous persons are endowed with a poor respiratory apparatus, and in these a hypotension is to be expected. The fall in arterial tension in advanced disease may be due to the dilatation of peripheral vessels resulting from a tuberculous toxemia. Tachycardia, which diminishes the systolic output of the heart, is another contributing factor. Cardiac dislocation, so frequently seen in advanced disease, may in itself be partly responsible for this permanent depression in arterial tension. The higher pressures observed in fibroid phthisis may be due to arteriosclerosis of the pulmonary vessels and to the frequent association of chronic bronchitis and emphysema in this form of tuberculosis. It appears that, regardless of the immediate prognosis, the blood-pressure remains stationary in about 50 per cent of all cases. Although some of the patients with favorable prognosis show a persistent increase in the arterial tension, the blood-pressure estimation alone is not a reliable indication of the immediate prognosis, because the pressure values increase in 24 per cent of definitely progressive patients. In this study tuberculosis was associated in 10 per cent of cases with essential hypertension. The hypertension did not in any way tend to aggravate the pulmonary condition. *Conclusions: 1:* The arterial tension in patients with minimal tuberculosis is within normal limits for individuals of the same sex and age. Blood-pressure determinations are, therefore, of little or no diagnostic value in incipient tuberculosis. *2:* The blood-pressure declines with the advance of the tuberculous process. Active cases almost invariably show a lower arterial tension than comparable quiescent cases. *3:* Patients with fibroid disease apparently show higher pressure values than those with other forms of tuberculosis. This is particularly noticeable in women over forty and is probably secondary to the influence of the menopause. *4:* The incidence of hemoptysis is greater in those with arterial tension below the average for their respective group than in those at or above the average. It appears, however, that the arterial tension and hemoptysis are not etiologically related. They are coincidental symptoms of advancing disease. Hemoptysis in the tuberculous with essential hypertension was seen less frequently than in cases with normal or subnormal blood pressure. *5:* The few patients under observation, in whom pulmonary tuberculosis and syphilis coexisted, had a higher blood-pressure and a more favorable immediate prognosis than patients free from syphilis. *6:* The development of an effusion and the induction of pneumothorax had no appreciable and permanent effect in altering the blood-pressure in either brachial artery as long as the intrathoracic equilibrium was not unduly disturbed as a result of mediastinal displacement. The mediastinal dislocation was prevented by early and judicious aspiration in the case of effusions and careful adjustment of the intrapleural pressure in pneumothorax cases with labile mediastinal structures. *7:* An increase or a decline in the blood-pressure of patients under treatment does not offer a reliable indication as to the course of the disease. However, it appears that the initial blood-pressure determinations are of some prognostic value. Those with higher arterial tension than the average for the age, sex and extent of involvement do better than those whose blood-pressure is below the average for the group.—*Observations on the Blood Pressure in Pulmonary Tuberculosis, B. P. Stivelman, Am. J. M. Sc., January, 1927, clxxiii, 46.—(U. E. Z.)*

Acoustics of Breath-Sounds.—Bronchial breath-sounds are formed by the movement of air columns through the bronchial tubes from the larynx to the bronchi of 5 mm. internal diameter. The manner of formation is essentially that for the formation of sounds in labial pipes. The nose, mouth and larynx condition vibrations of a frequency of 400 to 600 a second. The trachea conditions vibrations of a frequency of 800 per second. The main bronchi condition vibrations of 1,000 per second. These sounds are conducted along the lumina and in the walls and surrounding connective tissue of the walls toward the periphery of the chest. The sound within the lumen is nearly completely obliterated by friction when tubes of an internal diameter of about 2 mm. are reached. Only part of the sound energy of the expiratory bronchial breath-sound reaches the thoracic wall, being conducted along the walls of the tubes and through the strongly absorbing porous substance of the aveolar structure. Bronchi, with an internal diameter of 3 mm., are 3 cm. from the pleural surface in the upper lobes and 3.5 to 5 cm. from the pleural surface in the lower lobes, except near the vertebral column, where they are only from 1 to 2 cm. from the periphery. Consolidation must reach inward this far in order to make good conducting contact with bronchial tubes of 3 mm. bore, and thus conduct bronchial breath-sounds to the wall of the thorax in pneumonia. The first physical signs of pneumonia obtained on auscultation are crepitant râles, diminished or absent breath-sounds and diminished spoken voice. Tactile fremitus is also diminished at a time when the consolidation has not reached bronchi of 3 mm. internal diameter. There are bronchial breathing and bronchophony and a stronger fremitus when bronchi of this diameter are surrounded by consolidation reaching to the periphery. Pectoriloquy appears when the consolidation reaches to bronchi of 5 to 6 mm. internal diameter. The spoken vowel sound over a normal lung area contains only the fundamental frequency of the vowel sound. The condition of pectoriloquy is obtained when the vowel sound is so well conducted to the chest wall that the sound contains the formatives as well as the fundamental frequency of the vowel sound. Bronchophony is the condition in which the fundamental frequency is better transmitted to the periphery, and thus louder, but the formative or formatives are not well transmitted, and therefore the vowel is not distinct, but only louder than when heard over normal lung area.—*The Acoustics of the Bronchial Breath Sounds, G. Fahr., Arch. Int. Med., February, 1927, xxxix, 2.—(G. F. H.)*

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